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(54) Title: LIQUID TRANSFER SYSTEM			
(57) Abstract			
<p>A dropping tool for transferring drops of a liquid onto a substrate wherein a surface of the dropping tool for contact with the liquid has a first region which exhibits an affinity to the liquid to be transferred directly surrounded by a second region which exhibits a lower affinity to the liquid to be transferred than the first region; the topography of the first and second regions and the relative affinities of the first and second regions for the liquid to be transferred being selected such that when the dropping tool is dipped into and then removed from a source of the liquid to be transferred, the liquid adheres to the first region without substantially any adherence of the liquid to the second region. A dropping tool for transferring drops of liquid onto a substrate, the dropping tool comprising a tip, at least one surface tapered towards the tip, and a capillary channel which leads from a position of the tapered surface remote from the tip to a reservoir located within the dropping tool. A method for transferring drops of liquid carried on a dropping tool onto a substrate to form an ordered array of drops thereon wherein the drop of liquid is transferred without contacting the dropping tool with the substrate either directly or indirectly via the drop of liquid.</p>			

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LIQUID TRANSFER SYSTEM

The present invention relates to tools and methods for dispensing an ordered array of liquid drops onto a solid substrate, particularly for multiple testing in the biotechnological field.

In the biotechnological field, it is often necessary to dispense liquid drops in an ordered array onto a solid substrate for performing multiple tests. There has been a strong desire to reduce the size of each individual liquid drop transferred on to the substrate so as to be able to increase the density of dots per unit area of substrate and at the same time minimize the volumes of expensive reagents required for the tests.

It is an aim of the present invention to provide a dropping tool for dispensing drops of liquid on to a solid substrate which is of relatively simple construction and with which it is possible to dispense drops of relatively small size with excellent reproducibility.

It is another aim of the present invention to provide an alternative and improved method for transferring a drop of liquid carried on a dropping tool on to a target substrate.

According to a first aspect of the present invention, there is provided a use of a dropping tool in a method of transferring drops of liquid on to a substrate, wherein a surface of the dropping tool for contact with the liquid has a first region which exhibits an affinity to the liquid to be transferred directly surrounded by a second region which exhibits a lower affinity to the liquid to be transferred than the first region; the topography of the first and second regions and the relative affinities of the first and second regions for the liquid to be transferred being selected such that when the dropping tool is dipped into and then removed from a source of the liquid to be transferred, the liquid adheres to the first region without substantially any adherence of the liquid to the second region.

According to a second aspect of the present invention, there is provided a dropping tool for transferring drops of a liquid onto a substrate wherein a surface of the dropping tool for contact with the liquid has a first region which exhibits an affinity to the liquid to be

transferred directly surrounded by a second region which exhibits a lower affinity to the liquid to be transferred than the first region; the topography of the first and second regions and the relative affinities of the first and second regions for the liquid to be transferred being selected such that when the dropping tool is dipped into and then removed from a source of the liquid to be transferred, the liquid adheres to the first region without substantially any adherence of the liquid to the second region.

According to a third aspect of the present invention, there is provided a method for transferring drops of liquid carried on a dropping tool on to a substrate to form an ordered array of drops thereon wherein the drop of liquid is transferred without contacting the dropping tool with the substrate either directly or indirectly via the drop of liquid.

According to a fourth aspect of the present invention, there is provided a dropping tool for transferring drops of liquid on to a substrate, the dropping tool comprising a tip, at least one surface tapered towards the tip, and a capillary channel which leads from a position of the tapered surface remote from the tip to a reservoir located within the dropping tool.

Embodiments of the present invention will now be described hereunder, by way of example only, with reference to the accompanying drawings in which:-

Figures 1 to 15 are schematic cross-sectional views of the lower sections of dropping tools according to fifteen different embodiments of the present invention respectively.

Figure 1 shows a cross-sectional view of the lower section of a dropping tool according to a first embodiment of the present invention for transferring drops of an aqueous liquid onto a solid substrate. In this embodiment the dropping tool is a steel pin substrate 12 having its whole surface other than a region at its tip 14 coated with a layer 16 of a relatively hydrophobic material such as teflon or tetrahedral amorphous carbon (t.a.C). The exposed area at the tip 14 is preferably generally circular in shape when viewed down the axis of the pin from the tip of the pin, and its size is determined in

accordance with the desired drop size but will generally be of the order of a fraction of a mm, preferably about 0.1mm or less. In this first embodiment, the boundary between the exposed steel tip of the pin and the relatively hydrophilic coating is topologically continuous. This dropping tool can be fabricated by removing a small thickness of surface steel from the portion of the surface of a conventional steel dropping pin surrounding the tip of the pin followed by subsequent application of a layer of the relatively hydrophobic material onto the region of the pin from which the layer of steel has been removed. The removal of the layer of steel can be carried out by a mechanical process or by physical or chemical etching. The application of the layer of relatively hydrophobic material can, for example, be carried out by filtered vacuum arc (fcva), plasma enhanced chemical vapour deposition (pecvd), evaporation or by dipping the relevant portion of the pin in a liquid of the material. Plasma-enhanced chemical vapour deposition is the preferred method of application.

The selection of the material used for the relatively hydrophobic region will depend on the desired drop size. For example, particularly small tip sizes (for producing particularly small drops) will require the selection of a material which is much less hydrophilic than the exposed steel tip of the pin if the drop of liquid is to be contained within the bounds of the exposed hydrophilic tip of the dropping pin.

Figure 2 shows a cross-sectional view of the lower section of a dropping tool according to a second embodiment of the present invention for dispensing drops of an aqueous liquid on to a solid substrate. In this second embodiment, a pin substrate 22 made of a relatively hydrophobic material such as teflon is provided at its tip 24 with a thin circular layer 28 of a hydrophilic material such as platinum. As in the first embodiment, the boundary between the layer of hydrophilic material and the non-coated surface of the hydrophobic pin substrate is topologically continuous.

Figure 3 shows a cross-sectional view of the lower section of a dropping tool according to a third embodiment of the present invention for dispensing drops of an aqueous liquid onto a solid substrate. A steel pin substrate 32 is coated at its tip 34 with a thin layer 38 of a hydrophilic material such as hydrogenated amorphous carbon. and the region of the

pin surrounding the coated tip is coated with a thin layer 36 of a hydrophobic material such as teflon. As in the first two embodiments, the boundary between the hydrophilic tip and hydrophobic region surrounding the tip is topologically continuous. The layer 38 of hydrophilic material is preferably generally circular in shape when viewed down the axis of the pin from the tip of the pin.

Figure 4 shows a cross-sectional view of the lower section of a dropping tool according to a fourth embodiment of the present invention. This embodiment is similar to the first embodiment except that the layer 46 of relatively hydrophobic material is coated on a steel pin substrate 42 having a continuous surface such that there is a topological step at the boundary between the relatively hydrophobic layer and the exposed tip 44 of the pin in the resulting dropping tool. In other words, the relatively hydrophobic layer protrudes further than the underlying material. This makes it further energetically favourable for the liquid drop to terminate at the interface, and thus improves the uniformity of drop size.

Figure 5 shows a cross-sectional view of the lower section of a dropping tool according to a fifth embodiment of the present invention. This embodiment is similar to the second embodiment except that the layer of hydrophilic material 58 (such as platinum metal) is formed on the tip of a pin substrate 52 which is made of a relatively hydrophobic material (such as teflon) and has a continuous surface, with the result that there is a topological step at the boundary between the surface of the relatively hydrophobic pin substrate 52 and the hydrophilic layer 58. This has the same kind of advantages as those described for the fourth embodiment.

Figure 6 shows a cross-sectional view of the lower section of a dropping tool according to a sixth embodiment of the present invention. This embodiment is similar to the third embodiment except that the thickness of the layer 66 of relatively hydrophobic material is greater than the thickness of the layer 68 of the hydrophilic material resulting in a topological step at the boundary between the two layers. This construction also has the same kind of advantages as those described above for the fourth embodiment.

Figure 7 shows a cross-sectional view of the lower section of a dropping tool according to a seventh embodiment of the present invention. A pin-shaped substrate 72 has a layer 78 of a hydrophilic material such as hydrogenated amorphous carbon over its entire surface. A layer 76 of a relatively hydrophobic material such as teflon is formed over the entire surface of the layer of hydrophilic material except for a region 74 at the tip of the pin to leave the layer of relatively hydrophilic material exposed. The exposed region is preferably generally circular in shape when viewed down the axis of the pin from the tip of the pin.

Figure 8 shows a cross-sectional view of the lower section of a dropping tool according to an eighth embodiment of the present invention. A steel pin substrate 82 has a capillary channel 83 running vertically from its tip to a reservoir 85 located inside the steel pin substrate 82. The surface of the pin substrate 82 surrounding the entrance to the capillary channel 83 is coated with a thin layer 86 of a relatively hydrophobic material such as teflon. This construction allows for the transfer of a plurality of drops (for example, ten drops) of uniform size without having to revisit the source of liquid after the transfer of each drop.

The above-described dropping pins are used in the following manner. The dropping pin is dipped into and then removed from a source of the liquid to be transferred. A drop of liquid remains adhered to the hydrophilic tip of the pin but not to the relatively hydrophobic region surrounding the tip of the pin, ensuring that a liquid drop of uniform size is loaded onto the dropping pin each time the pin is dipped into and then removed from the liquid source. The liquid drop can then be transferred to a solid substrate in a number of ways. For example, it can be deposited by the conventional method of bringing the tip of the dropping pin into close proximity with the surface of the solid substrate such that the drop of liquid makes simultaneous contact with the surface of the solid substrate. Provided that the surface of the solid substrate is not less hydrophilic than the tip of the dropping pin, the drop of liquid transfers to the solid substrate when the dropping tool is then withdrawn from the surface of the solid substrate.

Alternatively, the liquid drop can also be transferred by the new transfer methods of the present invention. In one such method, the tip of the dropping pin is accelerated down towards the surface of the solid substrate and then stopped at a high rate of deacceleration at a position above the surface of the solid substrate where the drop of liquid does not make simultaneous contact with the surface of the solid substrate. The momentum of the liquid drop causes it to become projected from the tip of the pin on to the surface of the solid substrate.

In an alternative transfer method, the tip of the dropping pin is brought into a position above the surface of the solid substrate where the drop of liquid does not make simultaneous contact with the surface of the solid substrate. A pressure wave is then induced in the body of the pin such that it is focussed at the point of the pin where the liquid drop is being carried (i.e. the tip). The pressure wave causes the drop of liquid to become projected from the tip of the pin on to the substrate. The pressure wave can be created by physically tapping the end of the pin opposite to its tip or by other non-mechanical means such as piezoelectric or electromagnetic effects.

The two methods of the present invention described above have the advantage that it is not necessary to ensure that the tip of the pin is less hydrophilic than the surface of the solid substrate onto which the liquid drop is transferred, and the materials used to make the pin can therefore be selected regardless of the nature of the substrate onto which the drop of liquid is to be transferred.

Figure 9 shows a cross-sectional view of a dropping tool according to a ninth embodiment of the present invention. In this embodiment, a pin substrate having a squared-off tip is provided with a recess 97 at its tip. A layer 98 of a hydrophilic material is formed over the entire surface of the pin substrate 92, and a second layer 96 of a relatively hydrophobic material is formed over the entire surface of the layer 98 of hydrophilic material except for a circular (when viewed down the axis of the pin) region 99 in the recess 97 at the tip of the pin. The recess is preferably made deep enough that a drop of liquid carried on the hydrophilic region of the recess of the pin does not make contact with the surface of a solid substrate when the squared-off portion 94 of the tip of

the pin is brought into contact therewith. The drop of liquid can then be transferred from the pin on to the solid substrate by impacting the squared-off portion 94 of the tip of the pin with the surface of the solid substrate whereby the drop of liquid carried in the recess is projected from the pin onto the surface of the solid substrate by its own momentum. The drop of liquid could of course also be transferred by the two non-contact methods described above.

Figure 10 shows a cross-sectional view of the lower section of a dropping tool according to a tenth embodiment of the present invention. The steel dropping tool is wedge shaped with a squared-off tip 104 and a tapered face 101 tapered towards the squared-off tip 104. A capillary channel 103 extends from the tapered face 101 to a reservoir 105 located within the dropping tool. The capillary channel 103 is preferably formed so as to extend in a direction approximately perpendicular to the squared-off tip 104. The capillary channel 103 and reservoir 105 can be formed for example by electron discharge machining (EDM), laser ablation or by focussed ion beam etching. In use, the dropping tool is dipped into a source of the liquid to be transferred to fill the reservoir 105 and capillary channel 103. The squared-off tip 104 of the dropping tool is then impacted against the surface of the target solid substrate at an appropriate velocity such that a single drop of liquid is projected from the entrance of the capillary channel on to the surface of the solid substrate by a momentum effect.

Figure 11 shows a cross-sectional view of a dropping tool according to an eleventh embodiment of the present invention. This embodiment is identical to the tenth embodiment except that a layer 106 of relatively hydrophobic material such as teflon is formed on the entire surface of the dropping tool surrounding the entrance to the capillary channel 113. This deters liquid at the entrance to the capillary channel 113 from spreading onto the surrounding surface of the dropping tool whereby the uniformity of drop size can be further improved.

Figure 12 shows a cross-sectional view of a dropping tool according to a twelfth embodiment of the present invention. This embodiment is similar to the tenth embodiment except that it does not have a capillary channel leading from the tapered

surface to a reservoir. Instead, a layer 128 of hydrophilic material such as hydrogenated amorphous carbon is formed over the entire surface of the dropping tool, and a second layer 126 of relatively hydrophobic material, such as teflon, is formed over the entire surface of the layer of hydrophilic material except for a circular region 125 thereof on the tapered surface. When the dropping tool is dipped into a source of the liquid to be transferred, a drop of liquid adheres only to the exposed circular region 125 of the hydrophilic layer 128. The drop of liquid can then be transferred from the dropping tool to the target solid substrate by the impact method described above.

In Figures 10, 11 and 12, the entrance to the capillary channel (in the cases of Figures 10 and 11) or the region of hydrophilic material (in the case of Figure 12) is well separated from the tip of the dropping tool. However, it is also possible to have the same at a position much closer to the tip of the pin such that when the tip of the pin is brought into contact with a solid substrate, liquid carried at the entrance to the capillary channel or on the region of hydrophilic material makes simultaneous contact with the solid substrate and the dropping tool, whereby a drop of the liquid is transferred from the dropping tool to the solid substrate when the dropping pin is subsequently withdrawn from the solid substrate.

In each of the dropping tools described above, the size of the hydrophilic region of the surface of the tool or the size of the entrance to the capillary channel in the case of the eighth, tenth and eleventh embodiments is determined in accordance with the desired drop size. Desired drop sizes are typically of the order of a fraction of a mm, preferably about 0.1mm or less.

In the case of those embodiments which do not have a capillary channel, the dropping performance can be further improved by forming a third region of a relatively hydrophobic material at the centre of the hydrophilic region. A schematic cross-sectional view of such an embodiment is shown in Figure 13. A steel pin substrate 132 has a squared-off circular tip 138 having a diameter of about 0.1mm. The tapered surface of the pin substrate 132 leading towards the squared-off tip is coated with a thin layer 136 of a hydrophobic material. A small circular area at the centre of the squared-

off tip is coated with a thin layer 139 of a material which is less hydrophilic than the exposed surface of the steel pin but is preferably less hydrophobic than the layer 136 of relatively hydrophobic material surrounding the squared-off tip 138 of the pin. This third region functions to further ensure that the liquid is transferred from the dropping pin to the target substrate as a droplet.

Figure 14 shows a cross-sectional view of the lower section of a dropping tool according to a fourteenth embodiment of the present invention with a drop of an aqueous liquid carried on the pin. In this embodiment, an annular groove 145 is cut into a pin substrate 142 made of a relatively hydrophobic material (such as teflon) at a position distanced axially from the tip 144 of the pin. A layer of hydrophilic material such as hydrogenated amorphous carbon is applied to the groove to form a hydrophilic collar 148. The width of the collar 148 and the distance of the collar 148 from the tip of the pin is determined in accordance with the desired drop size. Desired drop sizes are typically of the order of a fraction of a mm, preferably 0.1mm or less.

When the dropping pin is dipped into and subsequently removed from a source of the aqueous liquid to be transferred, a drop of liquid remains adhered to the section of the surface of the dropping pin comprising the hydrophilic collar and the region at the tip of the pin encompassed by the hydrophilic collar.

Figure 15 shows a schematic cross-sectional view of a dropping pin according to a fifteenth embodiment of the present invention with a drop of aqueous liquid carried thereupon. This embodiment is similar in principle to the embodiment shown in Figure 14. A steel pin substrate 152 is first coated with a layer 156 of a relatively hydrophobic material such as teflon or tetrahedral amorphous carbon over its entire surface, and then an annular groove is then cut into the pin at a position distanced axially from the tip 154 of the pin to expose a collar of steel 155. As in the embodiment shown in Figure 14, the width of the collar and the distance of the collar from the tip of the pin is determined in accordance with the desired drop size.

The examples of dropping tools described in detail above are all designed for transferring drops of an aqueous liquid. However, all the above-described constructions can be adapted for use with any other kind of liquid such as organic liquids by appropriately selecting materials which have the corresponding relative affinities for the particular liquid to be transferred.

CLAIMS

1. Use of a dropping tool in a method of transferring drops of liquid on to a substrate, wherein a surface of the dropping tool for contact with the liquid has a first region which exhibits an affinity to the liquid to be transferred directly surrounded by a second region which exhibits a lower affinity to the liquid to be transferred than the first region; the topography of the first and second regions and the relative affinities of the first and second regions for the liquid to be transferred being selected such that when the dropping tool is dipped into and then removed from a source of the liquid to be transferred, the liquid adheres to the first region without substantially any adherence of the liquid to the second region.
2. A use of a dropping tool according to claim 1 wherein the dropping tool is a pin.
3. A use of a dropping tool according to claim 2 wherein the first region is located at the tip of the pin.
4. A use of a dropping tool according to claim 1 wherein the dropping tool has a tip and at least one surface tapered towards the tip, and wherein the first region is located at a position on the tapered surface remote from the tip.
5. A use of a dropping tool according to claim 1 wherein the boundary between the first and second regions is topologically discontinuous.
6. A use of a dropping tool according to claim 1 wherein the liquid to be transferred is an aqueous liquid, the first region is relatively hydrophilic and the second region is relatively hydrophobic.
7. A use of a dropping tool according to claim 1 wherein the first region is comprised of a first material having an affinity for the liquid to be transferred and the second region is comprised of a second material having a lower affinity for the liquid to be transferred than the first material.
8. A use of a dropping tool according to claim 1 wherein the first region of the dropping tool comprises a capillary channel leading to a reservoir located within the dropping tool, and the second region is located about the entrance to the capillary channel.

9. A use of a dropping tool according to claim 1 wherein the first region encompasses a third region which has an affinity to the liquid to be transferred which is less than that of the first region.
10. A use of a dropping tool according to claim 9 wherein the relative affinities of the first and third regions are selected such that the liquid is transferred to the substrate as a droplet.
11. A use of a dropping tool according to any preceding claim wherein the first region is of a size suitable for carrying a drop of liquid having a diameter of 1mm or less, preferably 0.1mm or less.
12. A dropping tool for transferring drops of a liquid onto a substrate wherein a surface of the dropping tool for contact with the liquid has a first region which exhibits an affinity to the liquid to be transferred directly surrounded by a second region which exhibits a lower affinity to the liquid to be transferred than the first region; the topography of the first and second regions and the relative affinities of the first and second regions for the liquid to be transferred being selected such that when the dropping tool is dipped into and then removed from a source of the liquid to be transferred, the liquid adheres to the first region without substantially any adherence of the liquid to the second region.
13. A dropping tool according to claim 12 wherein the first region is relatively hydrophilic and the second region is relatively hydrophobic.
14. A dropping tool according to claim 12 comprising a pin having a tip, and wherein the first region is located at the tip of the pin.
15. A dropping tool according to claim 12 comprising a tip and at least one surface tapered towards the tip, and wherein the first region is located at a position on the tapered surface remote from the tip.
16. A dropping tool according to any of claims 12 to 15 wherein the first region is of a size suitable for carrying a drop of liquid having a diameter of about 1mm or less, preferably 0.1mm or less.
17. A method for transferring drops of liquid carried on a dropping tool on to a substrate to form an ordered array of drops thereon wherein the drop of liquid

is transferred without contacting the dropping tool with the substrate either directly or indirectly via the drop of liquid.

18. A method for transferring a drop of liquid according to claim 17, the method comprising the steps of imparting a pressure wave to the dropping tool in such a manner that it travels through the body of the dropping tool and is focussed at the point of the dropping tool on which the liquid drop is carried to project the drop of liquid onto the substrate.
19. A method for transferring a drop of liquid according to claim 17, the method comprising the steps of accelerating the dropping tool towards the substrate, and then deaccelerating the dropping tool at a high deacceleration rate such that the drop of liquid carried on the dropping tool is projected from the dropping tool on to the substrate by virtue of its own momentum.
20. A method according to claim 17 wherein the dropping tool is a pin which is adapted to carry a liquid drop at its tip.
21. A method according to claim 20 wherein the pin has a capillary channel leading from its tip to a reservoir located inside the pin.
22. A method according to claim 17 wherein the dropping tool has a tip and at least one surface tapered towards the tip which is adapted to carry a liquid drop at a position remote from the tip.
23. A method according to claim 22 wherein the dropping tool has a capillary channel leading from a position of the tapered surface remote from the tip to a reservoir located inside the dropping tool.
24. A method according to claim 18 wherein the pressure waves are imparted mechanically or by a piezoelectric effect or electromagnetic effect.
25. A dropping tool for transferring drops of liquid on to a substrate, the dropping tool comprising a tip, at least one surface tapered towards the tip, and a capillary channel which leads from a position of the tapered surface remote from the tip to a reservoir located within the dropping tool.
26. A method of transferring drops of liquid on to a substrate using the dropping tool according to claim 25, comprising the steps of at least partially filling the capillary channel and reservoir with the liquid to be transferred, and impacting the tip of the dropping tool against the substrate so as to cause a drop of liquid

to be projected from the capillary channel on to the substrate by a momentum effect.

27. A method of transferring drops of liquid on to a substrate using the dropping tool according to claim 25, comprising the steps of at least partially filling the capillary channel and reservoir with the liquid to be transferred, and imparting a pressure wave to the dropping tool in such a manner that the pressure wave is focussed at the entrance of the capillary channel so as to cause a drop of liquid to be projected from the capillary channel on to the substrate.
28. A method according to any of claims 25 to 27, wherein an ordered array of liquid drops is formed on the substrate.
29. A use of a dropping tool as substantially hereinbefore described with reference to Figures 1 to 15 of the accompanying drawings.
30. A dropping tool as substantially hereinbefore described with reference to Figures 1 to 15 of the accompanying drawings.
31. A method for transferring drops of liquid on to a substrate as substantially hereinbefore described with reference to Figures 1 to 15 of the accompanying drawings.

AMENDED CLAIMS

[received by the International Bureau on 31 March 2000 (31.03.00);
original claims 1-31 replaced by new claims 1-27 (4 pages)]

CLAIMS

1. Use of a dropping tool in a method of transferring drops of liquid on to a substrate, wherein a surface of the dropping tool for contact with the liquid has a first region comprising a capillary channel leading to a reservoir located within the dropping tool and exhibiting an affinity to the liquid to be transferred, and a second region located about the entrance to the capillary channel and exhibiting a lower affinity to the liquid to be transferred than the first region; the relative affinities of the first and second regions for the liquid to be transferred being selected such that when the dropping tool is dipped into and then removed from a source of the liquid to be transferred, the liquid adheres to the first region without substantially any adherence of the liquid to the second region.
2. A use of a dropping tool according to claim 1 wherein the dropping tool is a pin.
3. A use of a dropping tool according to claim 2 wherein the entrance to the capillary channel is located at the tip of the pin.
4. A use of a dropping tool according to claim 1 wherein the dropping tool has a tip and at least one surface tapered towards the tip, and wherein the entrance to the capillary channel is located at a position on the tapered surface remote from the tip.
5. A use of a dropping tool according to claim 1 wherein the boundary between the first and second regions is topologically discontinuous.
6. A use of a dropping tool according to claim 1 wherein the liquid to be transferred is an aqueous liquid, the first region is relatively hydrophilic and the second region is relatively hydrophobic.
7. A use of a dropping tool according to claim 1 wherein the first region is comprised of a first material having an affinity for the liquid to be transferred and the second region is comprised of a second material having a lower affinity for the liquid to be transferred than the first material.

8. A use of a dropping tool according to any preceding claim wherein the capillary channel is of a size suitable for carrying a drop of liquid having a diameter of 1mm or less, preferably 0.1mm or less.
9. A dropping tool for transferring drops of a liquid onto a substrate wherein a surface of the dropping tool for contact with the liquid has a first region comprising a capillary channel leading to a reservoir located within a dropping tool and exhibiting an affinity to the liquid to be transferred, and a second region located about the entrance to the capillary channel and exhibiting a lower affinity to the liquid to be transferred than the first region; the relative affinities of the first and second regions for the liquid to be transferred being selected such that when the dropping tool is dipped into and then removed from a source of the liquid to be transferred, the liquid adheres to the first region without substantially any adherence of the liquid to the second region.
10. A dropping tool according to claim 9 wherein the first region is relatively hydrophilic and the second region is relatively hydrophobic.
11. A dropping tool according to claim 9 comprising a pin having a tip, and wherein the entrance to the capillary channel is located at the tip of the pin.
12. A dropping tool according to claim 9 comprising a tip and at least one surface tapered towards the tip, and wherein the entrance to the capillary channel is located at a position on the tapered surface remote from the tip.
13. A dropping tool according to any of claims 9 to 12 wherein the capillary channel is of a size suitable for carrying a drop of liquid having a diameter of about 1mm or less, preferably 0.1mm or less.
14. A method for transferring drops of liquid carried by a dropping pin onto a substrate to form an ordered array of drops thereon wherein a drop of liquid is transferred without contacting the dropping pin with the substrate either directly or indirectly via the drop of liquid.
15. A method for transferring a drop of liquid according to claim 14, the method comprising the steps of imparting a pressure wave to the dropping pin in such a manner that it travels through the body of the dropping pin and is focussed at the point of the dropping pin on which the liquid drop is carried to project the drop of liquid onto the substrate.

16. A method for transferring a drop of liquid according to claim 14, the method comprising the steps of accelerating the dropping pin towards the substrate, and then deaccelerating the dropping pin at a high deacceleration rate such that a drop of liquid carried on the dropping pin is projected from the dropping tool on to the substrate by virtue of its own momentum.
17. A method according to claim 14 wherein the pin has a capillary channel leading from its tip to a reservoir located inside the pin.
18. A method according to claim 14 wherein the dropping pin has a tip and at least one surface tapered towards the tip which is adapted to carry a liquid drop at a position remote from the tip.
19. A method according to claim 18 wherein the dropping pin has a capillary channel leading from a position of the tapered surface remote from the tip to a reservoir located inside the dropping pin.
20. A method according to claim 15 wherein the pressure waves are imparted mechanically or by a piezoelectric effect or electromagnetic effect.
21. A method of transferring drops of liquid on to a substrate using a dropping tool comprising a tip, at least one surface tapered towards the tip, and a capillary channel which leads from a position of the tapered surface remote from the tip to a reservoir located within the dropping tool, the method comprising the steps of at least partially filling the capillary channel and reservoir with the liquid to be transferred, and impacting the tip of the dropping tool against the substrate so as to cause a drop of liquid to be projected from the capillary channel on to the substrate by a momentum effect.
22. A method of transferring drops of liquid on to a substrate using a dropping tool comprising a tip, at least one surface tapered towards the tip, and a capillary channel which leads from a position of the tapered surface remote from the tip to a reservoir located within the dropping tool, the method comprising the steps of at least partially filling the capillary channel and reservoir with the liquid to be transferred, and imparting a pressure wave to the dropping tool in such a manner that the pressure wave is focussed at the entrance of the capillary channel so as to cause a drop of liquid to be projected from the capillary channel on to the substrate.

23. A method according to any of claims 14 to 19, wherein an ordered array of liquid drops is formed on the substrate.
24. Use of a dropping tool in a method of transferring drops of liquid on to a substrate, wherein a surface of the dropping tool for contact with the liquid has a first region which exhibits an affinity to the liquid to be transferred directly surrounded by a second region which exhibits a lower affinity to the liquid to be transferred than the first region; the boundary between the first and second regions being topologically discontinuous and the relative affinities of the first and second regions for the liquid to be transferred being selected such that when the dropping tool is dipped into and then removed from a source of the liquid to be transferred, the liquid adheres to the first region without substantially any adherence of the liquid to the second region.
25. A use of a dropping tool as substantially hereinbefore described with reference to Figures 1 to 15 of the accompanying drawings.
26. A dropping tool as substantially hereinbefore described with reference to Figures 1 to 15 of the accompanying drawings.
27. A method for transferring drops of liquid on to a substrate as substantially hereinbefore described with reference to Figures 1 to 15 of the accompanying drawings.

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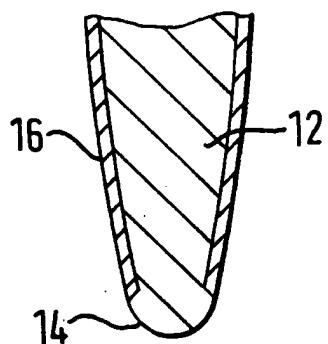


FIG. 1

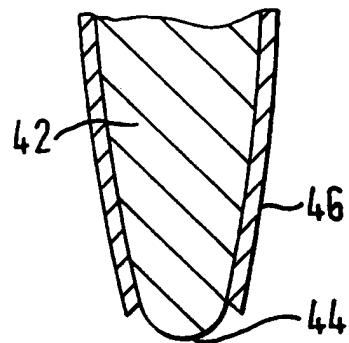


FIG. 4

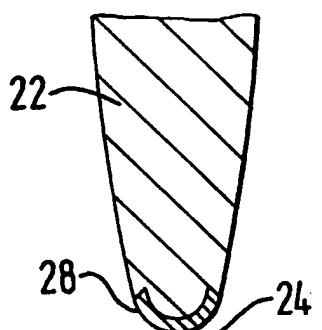


FIG. 2

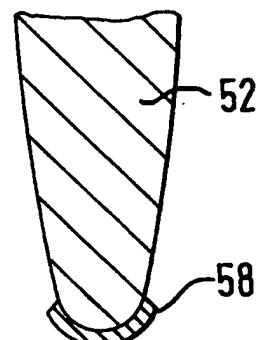


FIG. 5

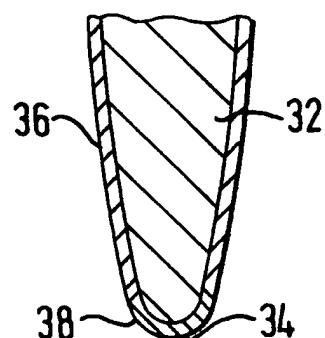


FIG. 3

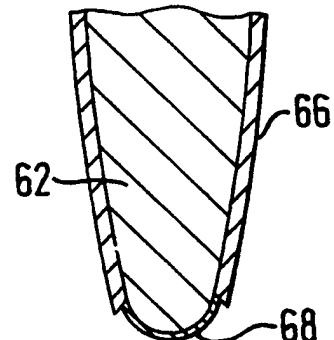


FIG. 6

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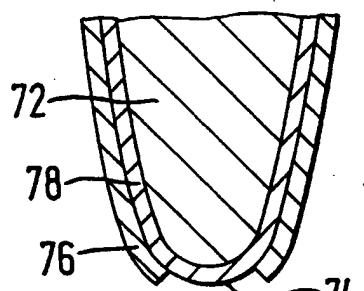


FIG. 7

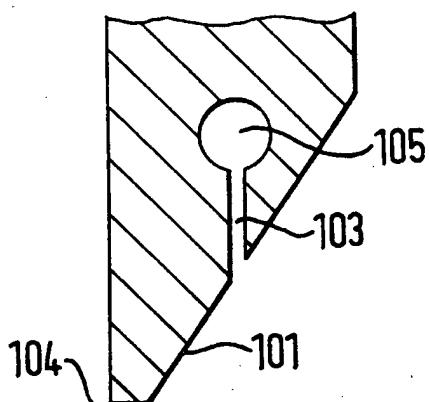


FIG. 10

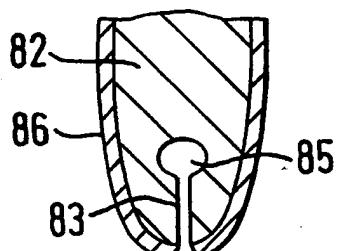


FIG. 8

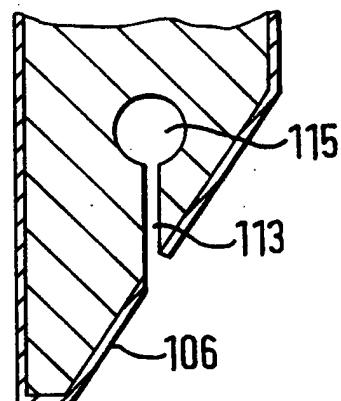


FIG. 11

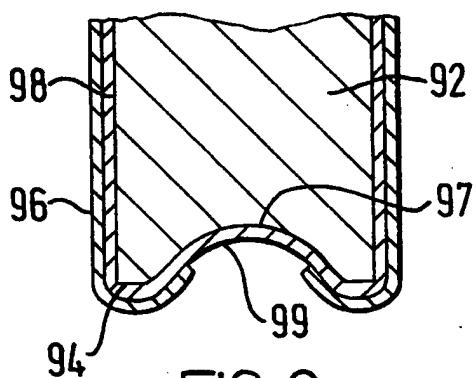


FIG. 9

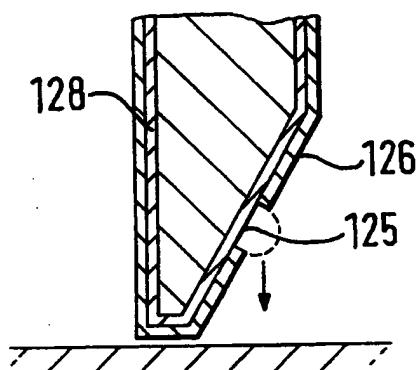


FIG. 12

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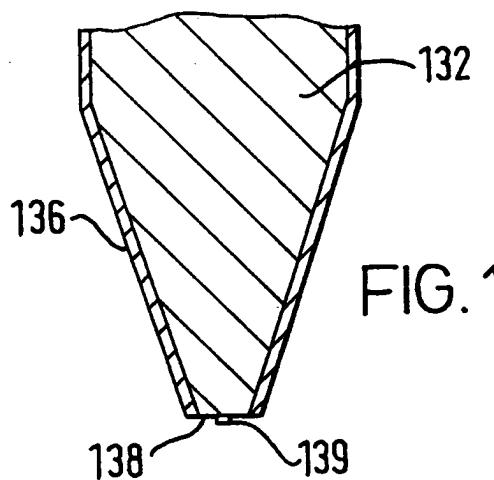


FIG. 13

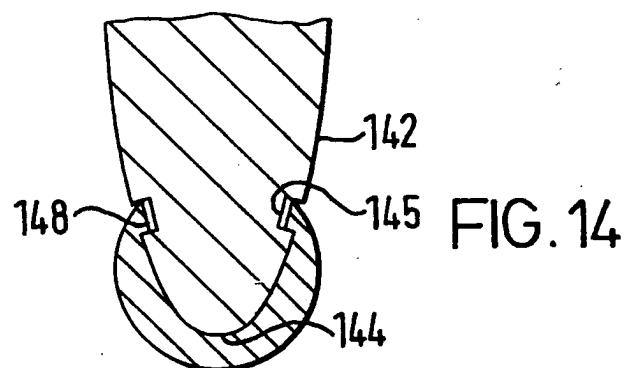


FIG. 14

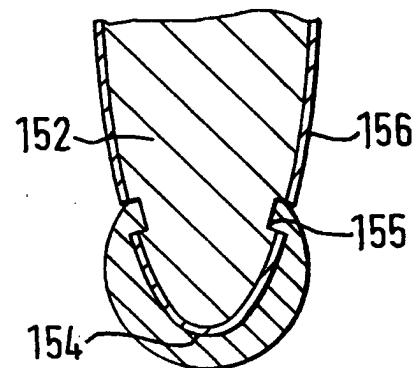


FIG. 15

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/03588

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 B01L3/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 B01L G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 756 050 A (ERSHOW GENNADY MOISEEVICH ET AL) 26 May 1998 (1998-05-26) abstract; figures 2-5 column 2, line 44 -column 3, line 59 column 4, line 19 -column 6, line 15	1-3, 6, 7, 11-14, 16
A	—	17, 25-27
X	EP 0 641 599 A (BOEHRINGER MANNHEIM GMBH) 8 March 1995 (1995-03-08) abstract; figure 2 page 2, line 50 -page 3, line 14 page 5, line 28 -page 5, line 31	1-3, 6, 7, 11-14, 16
A	—	17, 25-27
	—/—	

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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- "&" document member of the same patent family

Date of the actual completion of the international search

25 January 2000

Date of mailing of the international search report

01/02/2000

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INTERNATIONAL SEARCH REPORT

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PCT/GB 99/03588

C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 770 860 A (FRANZEN JOCHEN) 23 June 1998 (1998-06-23) abstract; figures 1,2 column 1, line 9 -column 1, line 21 column 2, line 58 -column 3, line 8 column 4, line 1 -column 4, line 19 column 6, line 58 -column 7, line 27	1-3,11, 12,14,16
A		6,7,13, 17,25-27
X	WO 98 15355 A (DANNOUX THIERRY L A ;CORNING INC (US)) 16 April 1998 (1998-04-16) abstract; figures 1-4 page 1, line 5 -page 1, line 10 page 2, line 23 -page 3, line 25 page 5, line 20 -page 7, line 17	1,6,7, 11-13,16
A		17,25-27
P,X	WO 98 57747 A (CORNING INC) 23 December 1998 (1998-12-23) abstract; figures 1-5 page 2, line 31 -page 5, line 13 page 6, line 7 -page 8	1-3,5-7, 11-14,16
A		17,25-27
X	US 5 334 353 A (BLATTNER FREDERICK R) 2 August 1994 (1994-08-02) abstract; figures 2-5 column 2, line 14 -column 2, line 25 column 2, line 60 -column 4, line 54 column 5, line 26 -column 5, line 64	17,19
A		18,20-27
A	US 5 763 278 A (BALMER JOHANNES KONRAD ET AL) 9 June 1998 (1998-06-09) abstract; figures 1-6 column 2, line 30 -column 2, line 62 column 3, line 15 -column 4, line 43	17-27
X	EP 0 768 519 A (JOHNSON & JOHNSON CLIN DIAG) 16 April 1997 (1997-04-16) abstract; figures 1,3,5 column 6, line 24 -column 6, line 47 column 3, line 55 -column 5, line 14	25
A		4,8,15, 21,22, 26,27
A	EP 0 364 203 A (PHYBER HOLDINGS LIMITED) 18 April 1990 (1990-04-18) abstract; figures 1-3 column 1, line 55 -column 2, line 31	4,8,15, 21-23, 25-27

INTERNATIONAL SEARCH REPORT

Interr. nat Application No

PCT/GB 99/03588

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
US 5756050 A	26-05-1998	RU	2041263 C		09-08-1995
		WO	9504594 A		16-02-1995
		US	5962329 A		05-10-1999
EP 0641599 A	08-03-1995	DE	4330412 A		09-03-1995
		AT	180184 T		15-06-1999
		DE	59408272 D		24-06-1999
		ES	2134298 T		01-10-1999
		JP	2672264 B		05-11-1997
		JP	7103799 A		18-04-1995
		US	5856200 A		05-01-1999
US 5770860 A	23-06-1998	DE	19628178 C		18-09-1997
		GB	2315329 A		28-01-1998
WO 9815355 A	16-04-1998	FR	2754469 A		17-04-1998
		AU	4747197 A		05-05-1998
WO 9857747 A	23-12-1998	FR	2764705 A		18-12-1998
US 5334353 A	02-08-1994	US	5525515 A		11-06-1996
US 5763278 A	09-06-1998	WO	9716251 A		09-05-1997
		EP	0876219 A		11-11-1998
EP 0768519 A	16-04-1997	CA	2187863 A		17-04-1997
		JP	9133676 A		20-05-1997
		US	5843793 A		01-12-1998
EP 0364203 A	18-04-1990	JP	2257034 A		17-10-1990